REMARKS/ARGUMENTS

I. Status of the Claims

Prior to entry of this amendment, claims 19-30 were pending, with claims 19, 20 and 29 withdrawn from consideration as drawn to non-elected subject matter. Upon entry of this amendment, claims 21, 23, 27-28 and 30 are amended and claims 19, 20 and 29 canceled without prejudice or disclaimer. These amendments do not limit the scope of the original claims and are made to improve readability and consistency in language. The amended claims are thus entitled to the full scope of equivalents as the original claims. Hence, after entry of this amendment, claims 21-28 and 30 are pending.

II. Amendments to Specification

Certain paragraphs have been amended to incorporate sequence identifiers. The amendment assumes that the amendments made in the September 13, 2002 amendment have been entered. The sequence identifiers were previously entered into the specification in the amendment filed October 17, 2001. But because they were omitted in the September 13, 2002 amendment, they are reintroduced now.

III. Rejection of Claims under 35 U.S.C. 112, Second Paragraph

Claims 21-28 are rejected as being indefinite because claim 21 recites to a first probe that differs between sets yet recites that the first probe is common to all the pools. It is thus concluded that it is unclear whether the first probe is different or the same within the pools.

It is initially noted in response that the rejection applies to claims 24-28; these claims do not depend upon claim 21 nor include the language that is objected to. It is assumed that the rejection was intended to be limited to claims 21-23. If this is not the case, clarification is requested. With respect to the merits of the rejection, it is noted that the first probes within the *same* set have the same sequence, whereas first probes in *different* sets have different sequences. Claim 1 has been amended to clarify this.

IV. Rejection of Claims under 35 U.S.C. § 103(a)

Claims 21-28 and 30 stand rejected as obvious over a published PCT application to Satoshi et al. (WO 98/11210) in view of U.S. Patent 6,103,463 to Chetverin et al. (hereinafter "Chetverin"). As an initial matter, Applicants note that the Satoshi PCT publication cited by the Examiner has matured into U.S. Patent 6,225, 056 (a courtesy copy is enclosed herein for the convenience of the Examiner). This is a more useful document for discussion because it is in English, whereas the PCT reference is in Japanese, with the exception of the abstract.

The Office Action says that Satoshi discusses an array with a first probe that binds to different mismatches at an interrogation site and a second probe that is common to the target sequence and nonoverlapping to the complementary region of the first probe. Chetverin is said to discuss arrays with different probes at different regions. The combined discussion in these two references is said to render the current claims obvious. For the reasons that follow, Applicants respectfully disagree.

A. Claim 21

The foregoing rationale does not seem pertinent to this claim does not make reference to interrogation probes. Nonetheless, even when the disclosures from both Satoshi and Chetverin are combined, they fail to teach or suggest each element of this claim as required to establish a prima facie case of obviousness.

For example, the array described in current claim 21 includes the following elements:

1. A plurality of sets of nucleic acid probes, each set comprising a plurality of probe pools;

2. Each pool of probes, in turn, includes (i) a first probe that is complementary to a known marker located in a target nucleic acid, and (ii) a second probe that differs in sequence from the first probe; and

3. The first probes within the *same* set have the same sequence, whereas first probes in *different* sets have different sequences.

Satoshi discusses various arrays having one or more pairs of probes. The probes in a pair have base sequences that can sequentially hybridize with a particular target nucleic acid. The probes are attached to linker that restricts their range spatially such that if the pairs of probes hybridize to the target they can be ligated together. There is no discussion in Satoshi, however, of an array that includes, for example, either element 1 or 3.

In Figure 3, for instance, Satoshi depicts an array in which there is a pool of probes that include a first probe that can hybridize to one segment of a target nucleic acid and a second probe that can hybridize to a second segment of the target nucleic acid. There is no discussion in Satoshi, however, to suggest that an array of this type includes a plurality of sets of nucleic acid probes, each set comprising a plurality of probe pools. Nor does Satoshi discuss arrays having a plurality of nucleic acid sets in which the first probe of each of the plurality of probe pools within the same set have the same sequence, whereas first probes within different sets have different sequences. Said differently, there is no indication that the array shown in Fig. 3 describes arrays that include either elements 1 or 3 above.

Figure 8 of Satoshi depicts an array in which there is a set of 5 probe pairs. Even if one assumes that these 5 sets of probe pairs constitute a set, there is no indication that the array includes a plurality of such sets as claim 21 requires (see element 1 above). Moreover, there is no discussion in Satoshi that the array shown in Fig. 8 is one in which first probes within a set have the same sequence, whereas first probes within different sets have different sequences (see element 3). So the array shown in Fig. 8 of Satoshi also lacks at least elements 1 and 3.

Chetverin discusses various types of binary arrays. Arrays of this type are characterized by having immobilized oligonucleotides, each oligonucleotide including a constant segment and a variable segment. But there is no discussion in Chetverin to compensate for the deficiencies in disclosure of Satoshi.

So even when the disclosures of both Satoshi and Chetverin are combined, they fail to teach each and every element of claim 21 as required to establish a prima facie case of obviousness.

B. Claims 24 and 30

The array described in claim 24 (and used in the method of claim 30) have the following elements:

1. A plurality of different nucleic acid probe mixtures;

2. Each probe mixture comprises an interrogation probe and a partner probe;

3. The interrogation probes are complementary to a first segment of a reference nucleic acid that contains an interrogation position and are identical to one another except at the interrogation position, with different interrogation probes having a different one of the four nucleotide bases at the interrogation position; and

4. The partner probe is complementary to a second segment of the reference nucleic acid that does not overlap the first segment; and

5. Different probe mixtures have different interrogation probes.

As noted supra, the Office Action contends that Satoshi discusses arrays with first probe that binds to different mismatches at an interrogation site of a target nucleic acid and a second probe that is complementary to a region of the target that does not overlap the binding site of the first probe. A full reading, however, demonstrates that Satoshi only discusses arrays that have pairs of probes that bind different segments of a target nucleic acid, with the probes being positioned such that members of the probe pair can be ligated once they hybridize to their respective segments on the target. It appears that the Examiner may be relying on the depiction of the matching and mismatched pairs in Figure 3 to substantiate the conclusion that Satoshi discusses arrays that include interrogation probes. The discussion concerning Figure 3, however, refers to arrays in general terms simply stating that the arrays contain "two kinds of probes each having a base sequence capable of hybridizing with th[e] specified oligonucleotide sequence" (col. 4, lines 50-55). Figure 3 thus simply illustrates how such probes interact under two different situations, namely when each probe pair is fully complementary to its binding sequence on the target, and the alternative situation when at least one of the probes is not fully complementary and there is a mismatch.

But Satoshi is bereft of any discussion concerning interrogation probes such as described in the claims 24 and 30. In particular, there is no discussion of arrays including interrogation probes in which: 1) the interrogation probes are complementary to a first segment of a reference nucleic acid that contains an interrogation position, 2) the interrogation probes are identical to one another except at the interrogation position, and 3) different interrogation probes have a different one of the four nucleotide bases at the interrogation position. Nor does Satoshi discuss arrays having different probe mixtures that differ, at least in part, by having different interrogation probes. Satoshi thus fails to discuss, for example, at least elements 3 and 5.

The disclosure in Chetverin fails to compensate for these deficiencies in the Satoshi. So even when the disclosures of these two references are combined, they fail to teach or suggest each element of claims 24 or 30.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,

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